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THE BEHAVIOUR OF RADIOACTIVE SULPHUR AFTER ITS EXTERNAL APPLICATION TO THE SKIN.

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In the past twenty years a new tool has appeared for the investigation of disease processes; namely, the radioactive isotopes. These several elements have been shown to resemble their stable counterparts in all chemical properties, and in most physical properties save for a difference in atomic weight and the instability of their existence. They have been found to disintegrate in a predictable fashion, and over a predictable period of time, giving rise eventually to a stable element of lower atomic number, together with a surplus of electrons (beta rays), and gamma ray emissions. The distinctive rate of breakdown of each radio-active isotope is recorded in terms of its "half-life"; that is, the period of time in which the element decays to half its original degree of radioactivity, as measured in millicuries. The radioactivity released during this disintegration can be used as a means of tracing the element, thereby recording the quantity, distribution and fate of the parent element. By analogy, one can then determine the behaviour of the stable isotope, and hence its probable function in the process under study.

The methods that we can now invoke for such a study fall into three main categories:

(i) *Physical:* By the use of various instruments—Geiger and scintillation counters—which are sensitive to the radiation emitted from the radioactive element, may be obtained a quantitative record of the material present *in vivo* in the site studied.

(ii) *Chemical:* The radioisotope may be artificially introduced into a radical of the molecule of the substance under study, thereby enabling the latter to be

traced during the course of its metabolism. The usefulness of this method depends upon the identity of the chemical properties of the radioactive and the stable isotopes. The resultant products of these metabolic processes may then be submitted to analysis by the instruments mentioned above, as an *in vitro* procedure.

(iii) *Autoradiography :* The radioactive discharge of the material can be recorded upon a photographic film, if the tissue or fluid is placed in contact with the emulsion under darkroom conditions. Since gamma rays, with their greater penetration, pass through such a film without impression, it is chiefly the beta rays that are recorded. Such a record is not quantitative. The test must be conducted entirely as an *in vitro* procedure, since it depends for its success on the close apposition of the two materials. In general, the method used for such a test is as follows :

(*a*) After routine biopsy, the tissue is cut in the usual histological fashion, either as a frozen section or after paraffin embedding.

(*b*) A monochromatic stain, such as eosin 1% is applied.

(*c*) The tissue section (or a smear of the concentrated fluid, if the material is liquid) is placed in contact with photographic film in a darkroom. This may be done in various ways :

(i) The tissue may be laid upon the photographic plate (Evans, 1947).

(ii) The film emulsion may be liquefied, and painted over the surface of the previously mounted section. (Leblond *et al.*, 1948).

(iii) Specially prepared nuclear track film may be stripped from its gelatin backing and laid like a blanket over the section (Pelc, 1947).

(*d*) The preparation is then stored in the dark, at a cool temperature for the duration of the exposure time.

(*e*) Photographic development is carried out as with ordinary film.

With each of these methods the position of a beta particle appears as a black spot at the site of its emission, while in the case of the last named film, there is in addition a black line accompanying the spot and registering the direction of subsequent motion of the particle.

Elemental sulphur has long been known as an effective agent in the treatment of various skin disorders, particularly seborrhoeic dermatitis, acne vulgaris, and psoriasis. It appears to function as a keratolytic and as a stimulant, but the mechanism by which these actions are produced has not so far been explained. Following its application to the skin, the sulphur has been shown to penetrate as a sulphide (Moncorps, 1929). Systemic effects may be demonstrated after such percutaneous absorption ; sulphaemoglobinaemia has been produced (Basch, 1926) ; increases in the serum glutathione levels may be observed (Lietha, 1942). These experimental results, coupled with the clinically

distinctive effects of sulphur, suggest that this element has a specific mode of action. With the availability of radioactive materials, an isotope of sulphur—S^{35}—has been produced, which will serve as a means of tracing the course of stable sulphur after its application to the skin surface. The only previous work using this isotope has been done after its incorporation into the lewisite molecule (Axelrod and Hamilton, 1947). In such a combination the sulphur will, of course, behave as lewisite, and this gives no indication of its behaviour as a separate substance.

In this investigation, then, we used the free elemental radioisotope for a threefold purpose :

(i) The demonstration, of the absorption and localization of sulphur in the normal skin ;
(ii) the observation of any alteration in the behaviour of the isotope in the presence of a dermatosis, particularly seborrhoeic dermatitis, acne vulgaris, and psoriasis ;
(iii) the demonstration of the effect of routine therapy of the lesions on the previously observed behaviour of the sulphur.

Methods.

Seventy patients were tested : 12 of these served as normal controls, 18 had seborrhoeic dermatitis, 18 acne vulgaris, 8 psoriasis, and the remainder a miscellany of conditions, including eczema, lichenification, ultraviolet irradiation, and discoid lupus erythematosus.

Radioactive sulphur S^{35}* with a half-life of 88 days was incorporated in hydrous emulsifying ointment (B.P.) together with 2% of stable sulphur (serving as a carrier). 100 mg. of the resultant preparation contained 5 microcuries of radioactivity. The ointment was applied with appropriate precautions to a 5 sq. cm. area of skin, and covered with a cellophane patch during the interval of contact.

Contact Geiger countings were taken before covering the area, and after removal of the patch at the end of the experiment. Control readings of the protective cover were also obtained.

Counts and biopsies were done at intervals of $\frac{1}{2}$, 2, 4, 8, 16, and 24 hours after the application of the radioactive material. (In the cases of acne vulgaris, further biopsies were done 2 and 3 weeks later.) The biopsies were frozen-sectioned, stained with 1% eosin, and then exposed, under dark-room conditions, to a nuclear track stripping film (Kodak). The resultant preparation was stored in a darkened container, at —4° C. for a period averaging 8 weeks. Development and fixation of the final product were carried out as with the

* S^{35} was obtained through the Department of Physics St. Bartholomew's Hospital Medical School (Professor J. Rotblatt).

ordinary photographic plate, using Kodak developer D19b and an acid fixer. A microscopic examination of the autoradiograph was then made.

The counting values yielded a quantitative measure of the sulphur retained in the skin, whilst the autoradiograph presented a visual record of its position and disposal.

Results.

Normal skin (Fig. 1). The absorption of S^{35} began two hours after its topical application ; within 8 hours it had completely traversed the epidermis, and was present in all layers. No preferential absorption through hair follicles or other naturally occurring appendiceal orifices was noted in any section, these

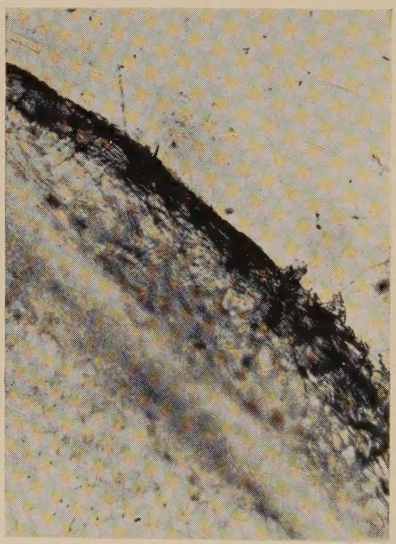

Fig. 1.—Autoradiograph of S^{35} in normal skin after 4 hours. The sulphur is present mainly in the stratum corneum. × 200.

merely sharing the burden of sulphur absorption with the rest of the unbroken epidermis.

After 16 hours, the greatest amount was demonstrable in the dermis, but no particular concentrations were noted near any structures such as sebaceous glands or blood vessels. From this point onwards, there was little if any sulphur in the epidermis. Within 24 hours, the sulphur had disappeared from the dermis as well, suggesting that its disposal was by systemic absorption. The quantities of radioactive material used were insufficient to permit detection in urinary excretion.

Microscopically, no obvious intracellular concentration of S^{35} was detected ; this suggests that transfer of the material was through intercellular substance.

When the test was repeated before or during the erythema phase of ultra-

violet therapy the mode of behaviour was unaltered but a much more rapid rate of penetration was noted. The entire absorption of sulphur was completed within 8 hours.

Seborrhoeic dermatitis (Fig. 2). Because of the possible excessive systemic absorption, no case of weeping dermatitis was tested. S^{35} applied to a typical seborrhoeic lesion began to penetrate within $\frac{1}{2}$ hour, and by 4 hours it was abundantly demonstrable within the outer portion of the epidermis. During the next 18 hours it concentrated in a linear distribution just deep to the midepidermis, but none entered the basal layers. Geiger counts done during this time recorded quantities approximately 10 times those measured in the normal. No deeper penetration of the sulphur was revealed by further biopsies.

FIG. 2.—Autoradiograph of S^{35} contained in the epidermis of a seborrhoeic lesion 4 hours after application. Notice the concentration of material in the mid-epidermis, and its tendency to intracellular localization. × 200.

Its disposal was accomplished by outward transfer during the next 4 to 12 hours.

Similar tests applied to the uninvolved skin of the same patients revealed no variation from the normal pattern.

Microscopic inspection of the sections showed an apparent intracellular concentration of S^{35}, sufficient in degree to permit the cell outlines to be traced by their content of the material.

Acne vulgaris (Fig. 3). Although the sulphur penetrated the epidermis as in the normal cases, a larger and more persistent concentration was observed in the hair follicles. This was possibly due to the relatively greater area in the latter which could provide an absorbing surface. Instead of the fairly rapid disappearance of the sulphur from the dermis that one saw in the normal skin, the material was observed to accumulate in the undischarged contents of the sebaceous glands. From the sections this sulphur appears to have three routes of ingress : first, *via* the hair follicles ; second, through the dermis, as shown

by the corresponding dermal accumulation of sulphur adjacent to the glands ; and third, by lateral diffusion through the epidermis, which appears to play a prominent role in those cases with associated seborrhoeic dermatitis. Once the sulphur had reached the lumen of the sebaceous gland it remained for as long as three weeks after the test was performed. This suggests that there is little absorption of sulphur in the reverse direction from the gland. Disposal of

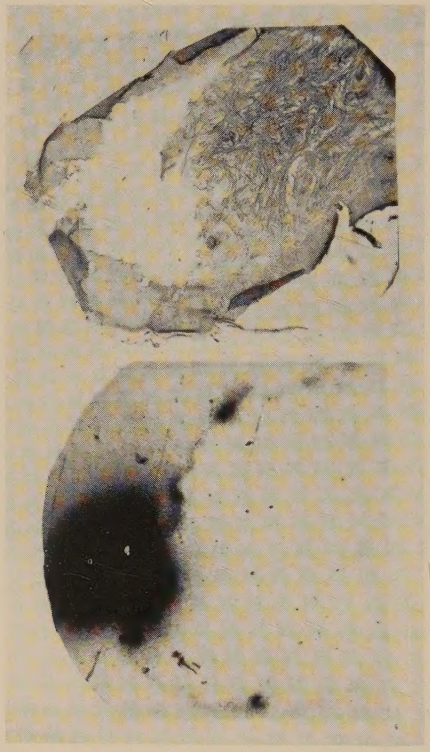

FIG. 3.—The upper photograph shows a section of skin stained in a routine manner (H. and E.) with a central sebaceous cyst whose wall has been ruptured externally. The lower picture is of the corresponding autoradiograph. Notice the dense black area representing S^{35} contained in the sebaceous material, and the black band of S^{35} in the position of the mid-epidermis. The section was prepared 18 hours after the external application of S^{35} to a skin with acne vulgaris and associated seborrhoeic dermatitis. × 30.

the sulphur remaining in the dermis was the same as in the normals. In those cases of acne with accompanying seborrhoeic dermatitis, the behaviour of the material in the epidermis resembled that seen in the seborrhoeic group.

Geiger counts directly over the sebaceous glands gave readings of 40%, 10 times the value obtained in the normal ; depending on its state, the adjacent skin yielded values within the range of those in normal and seborrhoeic skin.

Psoriasis (Fig. 4). Within 4 hours of its external application to a typical psoriatic lesion, S^{35} was seen to have penetrated as far as the basal layer of the

epidermis, and was present in all layers in sufficient quantity to yield counts of radioactivity 20 to 40 times that encountered in the normal. Relatively little entered the dermis, the greater proportion passing outwards again through the epidermis, possibly associated with the process of keratinization. All sulphur had disappeared by the end of 16 hours.

As in the case of the seborrhoeic lesion, an intracellular localization of the absorbed sulphur was noted on microscopic examination.

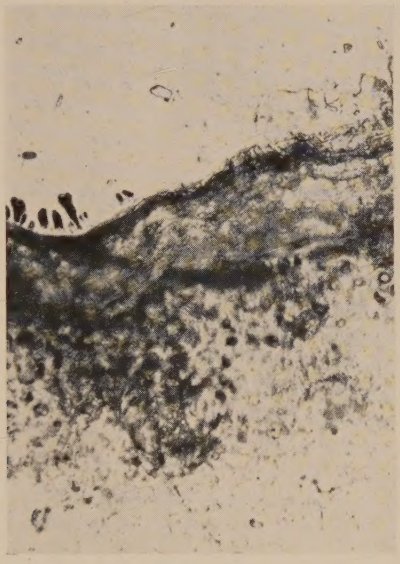

FIG. 4.—Autoradiograph of S^{35} in a psoriatic lesion 4 hours after external application. Notice that it is present in all layers, especially the basal one where it appears to be intracellular. × 200.

Uninvolved skin showed no deviation from the normal pattern (Table I).

Miscellaneous group. Cases of contact dermatitis, neurodermatitis, and discoid lupus erythematosus were tested to serve as controls for the seborrhoeic lesions. No skin denuded of epithelium was tested.

Sulphur applied in these lesions began its penetration in $\frac{1}{2}$ hour and reached the basal layer by the end of 4 hours. At no time was there observed any regional concentration of S^{35}. The material remained in the epidermis for up to 18 hours before its final disposal. Some of the sulphur was eliminated by outward transfer, and the remainder entered the dermis and was absorbed systemically. External Geiger counts of the skin during the sojourn of the sulphur therein remained within the limits of the range of values found in the normal skin.

Microscopically, no intracellular localization of the sulphur was detected.

Several cases of lichenification were tested in order to compare the results with those obtained in the cases of psoriasis. Here sulphur penetration did

TABLE I.—*The Behaviour of Sulphur* (35) *in Normal and Abnormal Skin.*

Type of skin.	Epidermis. Time of penetration (hr.).	Total sojourn (hr.).	Localization.	Cellular relation.	% activity present.	Final depth.	Disposal—main route.
Normal	2–8	16	None specific	Extra-	1–4	Dermis	Systemic absorption.
Seborrhoeic dermatitis	½–4	18	Stratum granulosum	Intra-	10–40	Mid-epidermis	Outward transfer.
Acne vulgaris	2–8	8	Sebaceous glands	Extra-	1–4	Dermis	Systemic absorption, gland discharge.
Psoriasis	½–4	16	Basal layer	Intra-	40	Basal layer	Outward transfer.
Eczema	½–4	18	Non-specific	Extra-	1–4	Dermis	Systemic absorption.
Lichenification	8–36	same	Non-specific	Extra-	1–4	Dermis	Systemic absorption.
Clearing seborrhoeic dermatitis	½–4	8	Basal layer	Intra-	1–4	Basal layer	Outward transfer.
Cleared seborrhoeic dermatitis	as in normal						

not begin until 6–8 hours after its application, and only after 36 hours had it reached the dermis from which it was systemically absorbed. The small quantity that remained in the epidermis was eliminated by passage to the surface. Thus the normal pattern of behaviour for S^{35} was reproduced albeit on a slower scale. These results are shown graphically in Fig. 5.

The Effect of Therapy on the Behaviour of S^{35}. The tests were repeated during the course of improvement in the lesions with therapy.

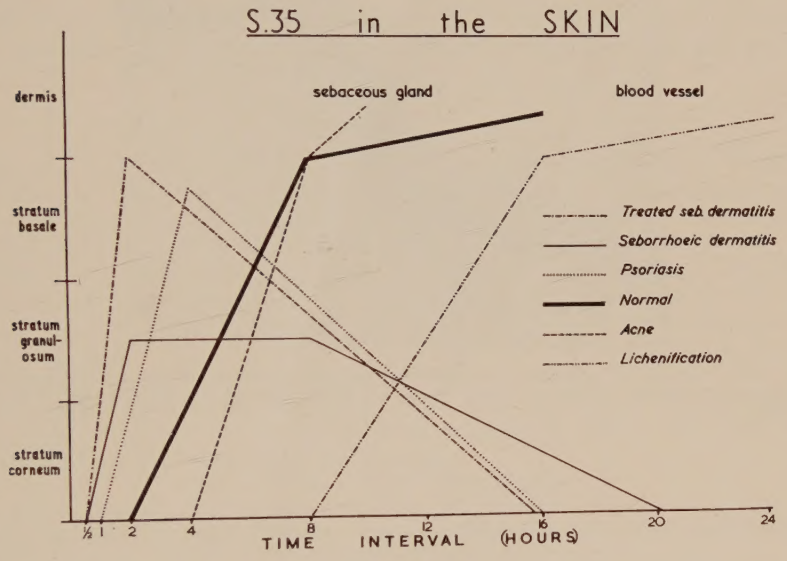

Fig. 5.

Seborrhoeic dermatitis. As improvement occurred, the depth to which S^{35} was able to penetrate gradually increased, until the basal layer was reached. Simultaneously, the tendency of the material to concentrate in the mid-epidermis disappeared, and the quantities detected by external counting methods returned to near-normal values. Until the point when the sulphur was able to pass the epidermal-dermal barrier, disposal was entirely by outward passage, but once it was able to enter the dermis it was absorbed systemically. Repeat tests done after the area was clinically normal revealed a normal mode of behaviour on the part of the sulphur. The time when the autoradiographic tracings became normal again seemed to coincide with the clearing of the lesion to naked-eye inspection, and at this point also the tendency of the sulphur to intracellular localization ceased (Fig. 6.)

Acne vulgaris. In those cases uncomplicated by coexistent seborrhoeic dermatitis, no discernible difference was noted in sulphur localization ; patients with associated seborrhoeic dermatitis showed the reversion to normal described

above. As long as enlarged sebaceous glands persisted, the S^{35} still tended to accumulate in their contents.

Psoriasis. In the cleared psoriasis lesion, the sulphur pattern had also returned to normal. During the course of treatment the epidermal concentration of the material fell to normal and the proportion of sulphur systemically absorbed increased.

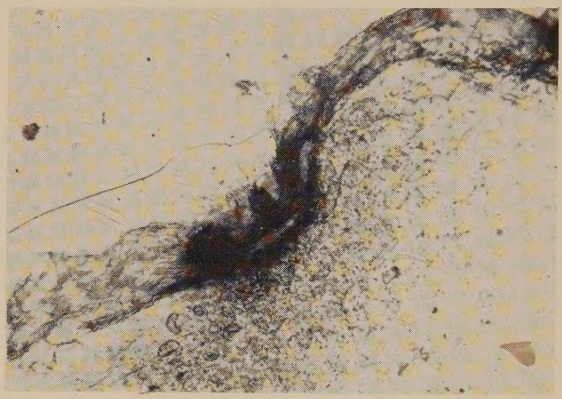

FIG. 6.—Autoradiograph of S^{35} in the partially cleared seborrhoeic lesion. The dense band of the mid-epidermis is still present, but S^{35} is detectable in the deeper layers as well. × 200.

DISCUSSION AND CONCLUSIONS.

Sulphur, as shown by autoradiographic visualization, is able to penetrate readily through the normal epidermis. There appears to be no preferential site of absorption through the appendages.

S^{35} shows an obvious difference in its pattern of behaviour in the various dermatoses investigated. This alteration in site of localization and mode of distribution occurs in a predictable fashion for each type of disease and parallels, in its return to normal, the clinical improvement in the lesion.

On the basis of these tests there appears to be no abnormality, as far as the anatomical distribution of sulphur is concerned, in the uninvolved skin of the same patient or in the area of a previous lesion.

Sulphur is known to be present in two main chemical groups in the skin; in the molecules of chondroitin sulphuric acid and mucoitin sulphuric acid, components of the intercellular ground substance; and in the intracellular epidermal proteins, having disulphide or sulphydryl groups (e.g., methionine, cystine, and cysteine).

Microscopic examination of the autoradiographs in these experiments demonstrated that in the normal skin, and in the skin of lichenification, eczema, and discoid lupus erythematosus, the sulphur remained entirely extracellular, while in the cases of seborrhoeic dermatitis and psoriasis it became intracellular.

Does this suggest that in the normal and miscellaneous groups the sulphur is absorbed through the intercellular substance of the skin, but that in seborrhoeic and psoriatic skin it becomes involved in an intracellular system containing sulphydryl and disulphide groups ?

Finally, the striking tendency of S^{35} to concentrate immediately deep to the midepidermis should be remarked. The location of the band thus formed is reminiscent of the so-called " keratogenous zone " of Giroud, which stains so densely with the Barrnet-Seligman stain for sulphydryl groups. Does this also suggest that sulphur is involved in an intracellular sulphydryl-containing enzyme system ? Is this its mechanism of action in seborrhoeic dermatitis ?

Summary.

A study was undertaken to trace the behaviour of radioactive sulphur when applied to the skins of normal subjects, cases of seborrhoeic dermatitis, acne vulgaris, psoriasis, and a miscellany of other dermatoses. Geiger counting was used to obtain quantitative values, and autoradiography to observe the localization of the material.

A distinctive pattern of behaviour for S^{35} was demonstrated in each of the three chief groups of dermatoses, differing from that seen in the normal. In addition quantitative measurements revealed 10 to 20 times the amount of sulphur present in the normal skin. Both the mode of behaviour and the quantities of S^{35} reverted to normal with clinical improvement in the lesions studied.

Several interesting features were noted, including the cellular relationship of the sulphur and its epidermal concentration in seborrhoeic dermatitis. The possible implications of these observations are discussed.

I should like to thank Dr. R. M. B. MacKenna for his suggestion to carry out this investigation and his supervision of the experimental work ; and, in addition, Mrs. E. Lloyd of the Physics Department for her co-operation in the physical counting methods used.

References.

Axelrod, D. J. and Hamilton, J. G. (1947) *Amer. J. Path.*, **23**, 389.
Basch, F. (1926) *Arch. exp. Path. Pharmak.*, **111**, 126.
Evans, T. C. (1947) *Proc. Soc. exp. Biol. Med., N.Y.*, **64**, 313.
Leblond, C. P., Percival, W. L. and Gross, J. (1948) *Proc. Soc. exp. Biol. Med., N.Y.*, **67**, 74.
Lietha, P. (1942) *Schweiz. med. Wschr.*, **72**, 650.
Moncorps, C. (1929) *Arch. exp. Path. Pharmak.*, **141**, 80.
Pelc, S. R. (1947) *Nature, Lond.*, **160** 749.

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THE VASCULAR LESION IN VISCEROCUTANEOUS COLLAGENOSIS.

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Systemic lupus erythematosus, generalized scleroderma and dermatomyositis are relatively rare syndromes, but are now diagnosed more often, no doubt owing to an increased awareness of their existence. As more cases are recognized intermediate variants are found which have widely differing clinical features and do not exactly fit into any one syndrome ; but when the tissues are examined histologically, common features are identified which seem to indicate that a common aetiology may exist (Klemperer, Pollack and Baehr, 1942 ; Banks, 1941 ; Baehr and Pollack, 1947). Pagel and Threip (1955), have drawn attention to these ill-defined states and, having coined the term Viscerocutaneous Collagenosis, have included them all in one class with systemic lupus erythematosus, generalized scleroderma and dermatomyositis.

It is intended in this paper to present some further cases showing features common to one or more of these syndromes and to analyse the vascular lesions that characterize them. It will be shown that some of the changes may be explained by the thrombosis hypothesis of Duguid (Duguid, 1946 ; 1948 ; 1949 ; 1954 ; 1955 ; Crawford and Levene, 1952 ; Duguid and Robertson, 1955).

Case Reports.

Case 1.—A girl aged 16developed a rapidly progressive erythematous skin lesion starting on the nose and cheeks and spreading to the trunk and limbs, accompanied by arthritis and hyperpyrexia. She died in 5 months without responding to cortisone therapy. L.E. cells were demonstrated on two occasions.

Necropsy.—Scaly red plaques were present over most of the face, trunk and limbs. There was a small infarct in the upper lobe of the right lung, a serous effusion in the pericardial sac and a small localized area of acute inflammation associated with a lesion in one of the branches of the left coronary artery. The myocardium under this latter lesion was necrotic.

Histology.—The skin lesions were typical of acute lupus erythematosus. One branch of the left coronary artery showed an acute focal periarteritis with thrombosis, the adjacent pericardium and muscle being necrotic. The area of infarction in the lung was associated with periarteritis and blockage of a branch of the pulmonary artery by fibrin or protein coagulum. The spleen showed laminated thickening of periarterial connective tissue, and many of the arterioles contained hyaline material both in the lumen and beneath the endothelium. Many of the capillaries in the renal glomeruli and juxta-glomerular arterioles were blocked by granular acidophilic material morphologically identical with that seen in " fibrinoid necrosis ".

Case 2.—A woman aged 47 who suffered for many years from severe Raynaud's disease developed dysphagia with loss of weight and dyspnoea on effort. This was associated with thickening of the skin of her forearms and hands. Barium swallow and oesophagoscopy showed an inert and pipe-like oesophagus. The dysphagia progressed, her fingers became blue and cold and terminally she developed oliguria. She died in congestive heart failure one year after the onset of dysphagia. L.E. cells were not found.

Necropsy.—The skin of the forearms and hands was scaly but not obviously thickened. There was gangrene of the tips of all fingers. The oesophagus was narrowed and the wall thickened. The pleura and pericardium were thickened and opaque. The kidneys showed multiple pale areas scattered throughout both cortex and medulla.

Histology.—The skin of the forearms showed changes compatible with both scleroderma and systemic lupus erythematosus. Many dermal arterioles were partly blocked by acidophilic hyaline material and many showed thickening of the walls. The tips of the fingers showed complete necrosis and the small arterioles were completely blocked by acidophilic structureless material. The oesophageal wall was thickened ; the mucous membrane was intact but the submucous coat was increased in width by chronically inflamed hyaline tissue while the muscle was atrophic and in parts necrotic. Many arterioles in the oesophagus showed thickening of their walls and some of them, together with the capillaries, were blocked by granular acidophilic material.

Both lungs showed acute broncho-pneumonia and many of the alveolar capillaries were blocked by hyaline or granular acidophilic material, this feature being most marked at the periphery of the lobes. The pleura and pericardium were thickened and chronically inflamed. The arterioles of the Malpighian bodies of the spleen were surrounded by zones of laminated connective tissue 5–6 layers thick. Both kidneys showed irregular cortical scarring and focal tubular necroses accompanied by multiple occlusive vascular lesions in the interlobular arteries and glomerular capillaries, there being partial or total blockage of the lumina by hyaline or acidophilic fibrinoid material or thickening of the intima.

Case 3.—A woman aged 37 developed stiffness and painless swelling of joints and, 9 months later, dysphagia accompanied by thickening of the skin. This became firm, tense and shiny, and latterly there was marked muscle wasting. L.E. cells were demonstrated in the peripheral blood. Her illness was progressive with but one short remission and she died 18 months after the onset.

Necropsy.—The skin of the face, trunk and arms was thickened, tense and indurated, and the skeletal muscles were all abnormally pale and friable. The oesophagus was thickened. The pleurae on both sides and the pericardium were thickened and opaque and there were multiple adhesions. The myocardium showed focal fibrosis.

Histology.—The skin, tongue and oesophagus showed changes typical of scleroderma. The skeletal muscles showed focal acute and chronic inflammation with diffuse atrophy and necrosis of individual fibres. Some of the arterioles associated with these were partly blocked with hyaline or fibrinoid material and many showed thickening of their walls.

The pleura and pericardium were thickened with chronic inflammation. Both lungs showed acute bronchopneumonia and several of the pulmonary arteries contained hyaline or fibrinoid material in their lumina. There was focal perivascular fibrosis in the myocardium and the interlobular arteries of both kidneys were partly or totally blocked by acidophilic granular material.

The three cases had histological changes common to all, but the organs involved differed. In all three, the skin, kidneys, spleen, pleura and pericardium were involved ; in two, the heart and oesophagus. In one case the skeletal muscle was damaged, and in another the fingers. The changes

involved both proliferation and various degenerative changes of the connective tissue, and also various lesions in the blood vessels. Some of the vascular lesions were recent, others were obviously of long standing, and it was in relation to the latter that the most striking connective tissue alteration was seen.

The more acute arterial lesions tended to be associated with oedema, exudates and necroses of the surrounding connective tissue, from which it seemed evident that the vascular lesions were the determining ones.

Single cross sections of affected vessels were often misleading since they did not give a comprehensive picture of the lesion and serial sections were therefore studied in most instances.

In many of the large arteries in the lung, muscle, oesophagus and skin the lumina were totally or partly blocked by fibrin or hyaline acidophilic material (Fig. 1). In other arteries of similar size the lumina were narrowed by organizing hyaline or cellular connective tissue (Fig. 2) or fibrous tissue producing thickening of the intima (Fig. 6). In comparing these lesions it was possible to trace a sequence starting with the deposition of fibrin or protein coagulum in the lumen (Fig. 1) ; this in turn became covered with endothelium and gradually organized (Fig. 2) so as to be transformed into a fibrous thickening of the intima with narrowing of the lumen (Fig. 6). In Case I a branch of the coronary artery and also one branch of a pulmonary artery were blocked by a cellular thrombus, and in both the intima, media and adventitia were infiltrated by polymorphs and round cells and were almost completely necrotic ; these changes are morphologically similar to those seen in periarteritis nodosa (Fig. 9).

The most prominent feature in the small arteries and arterioles was the presence of hyaline or granular acidophilic material, morphologically resembling fibrin or protein coagulum partly or totally occluding the lumen (Fig. 3). In most cases this material was adherent to the endothelium and contained round cells and polymorphs, but sometimes the material was lying beneath the endothelium (Fig. 4) or deep in the intima (Fig. 5) in such a way as to suggest that it had originally been present in the lumen. Further study of other small arteries suggested that the final stage was the conversion of this acidophilic material into fibrous intimal thickening with narrowing of the lumina (Fig. 6). In the renal glomeruli, lungs, oesophagus, skin and muscle similar hyaline or granular acidophilic material often completely or partly blocked the capillaries (Fig. 7) and occasionally there was thickening of the capillary walls by similar material which had obviously originated in the lumina (Fig. 8).

Discussion.

These three cases differed clinically and if they were classified according to accepted criteria the first would be taken as systemic lupus erythematosus, the second scleroderma, or on histological grounds as systemic lupus

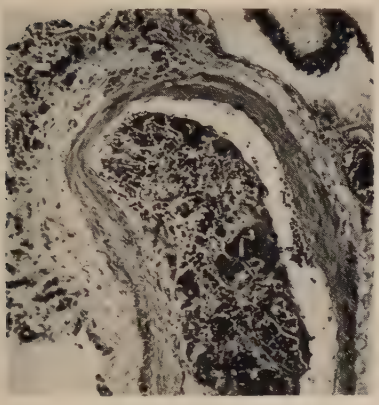

FIG. 1.—Pulmonary artery (Case 1) showing acidophilic hyaline material and cells almost completely blocking the lumen. H. & E. × 80.

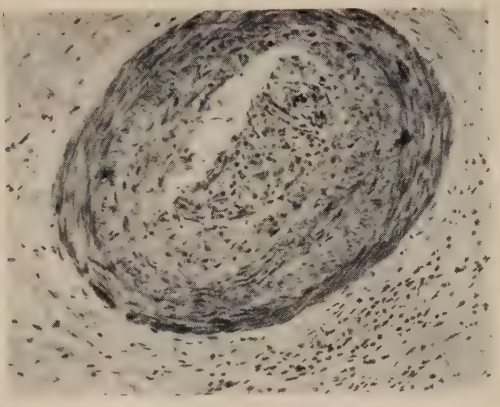

FIG. 2.—Artery in wall of oesophagus (Case 2) containing a cellular, partially organized tissue almost completely blocking the lumen. H. & E. × 160.

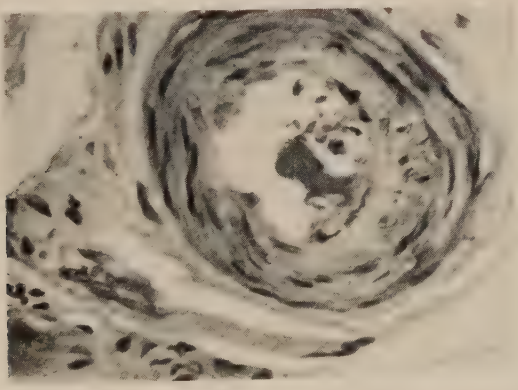

FIG. 3.—Dermal artery (Case 2) showing hyaline acidophilic material partly blocking the lumen. H. & E. × 160.

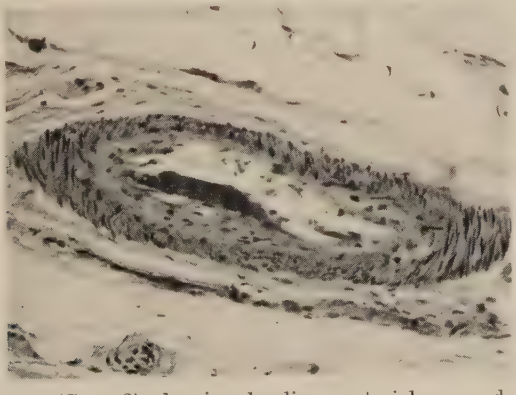

FIG. 4.—Dermal artery (Case 2) showing hyaline material covered with endothelium producing eccentric narrowing of the lumen. H. & E. × 160.

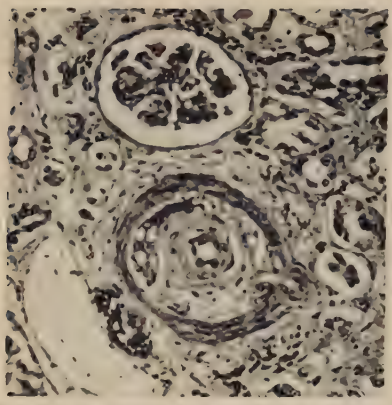

FIG. 5.—Interlobular artery of the kidney (Case 2) showing hyaline acidophilic material lying deep in the thickened intima. H. & E. × 240.

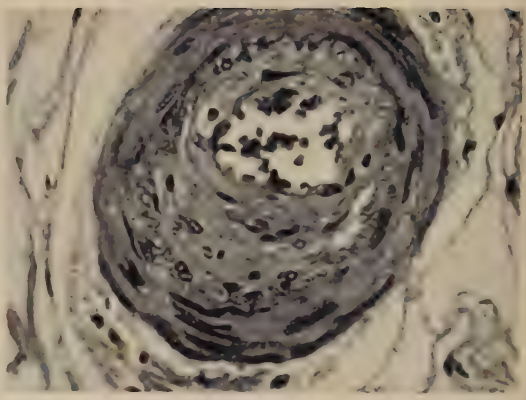

FIG. 6.—Oesophageal artery (Case 3) showing eccentric fibrous thickening of the intima. H. & E. × 380.

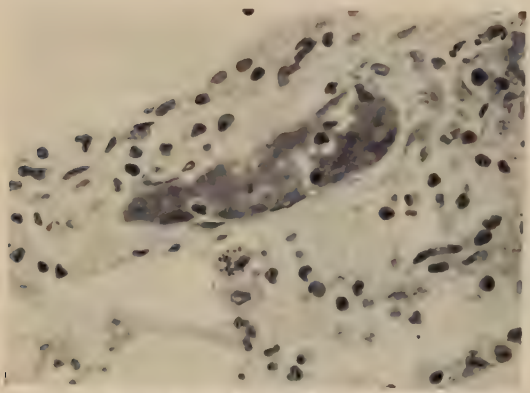

FIG. 7.—Alveolar capillary (Case 2) showing the lumen completely blocked by granular acidophilic material. H. & E. × 380.

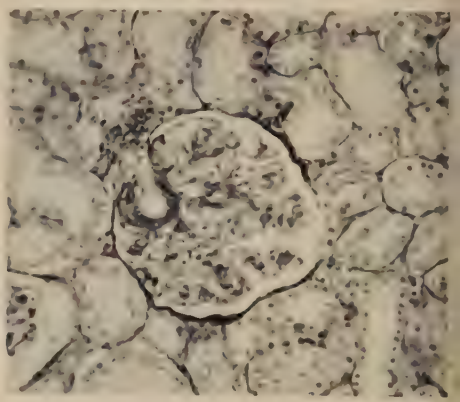

FIG. 8.—Glomerulus (Case 3) showing thickening of a capillary wall. Periodic Schiff. × 160.

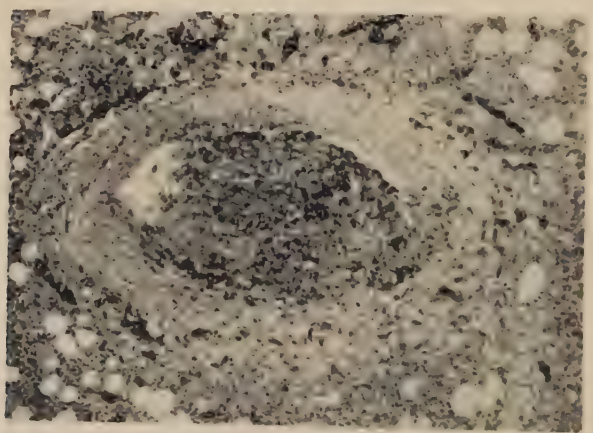

FIG. 9.—Coronary artery (Case 1) showing periarteritis with occlusion of the lumen by a cellular thrombus. H & E. × 120.

erythematosus and scleroderma, while the third might be taken as scleroderma but on a histological basis it resembled dermatomyositis. The finding of L.E. cells in this case linked it with the first. All three cases showed the same underlying histology and were obviously examples of one disease process and to split them into separate categories would be to confuse the problem.

As Pagel and Treip have suggested, there is much to be gained by adopting such a term as Viscerocutaneous Collagenosis to include them all if we could be sure what the the term " collagenosis " implies. The vascular lesions were prominent in all cases and if I interpret them correctly they consist of total or partial occlusion of the lumina by fibrin or protein coagula, which in time are converted into intima thickenings.

Duguid (1954) and Rannie and Duguid (1953) have demonstrated experimentally that solid matter deposited in the lumen of an artery is incorporated into the intima by a rearrangement of the endothelial lining, and Williams (1955) has shown how rapid this reaction can be. The appearances seen at different stages of the process are very different and many of them may be mistaken for degeneration. The lesions in the coronary and pulmonary arteries in Case 1 were identical with those produced in the lungs of rabbits by intravenous injections of autogenous or heterologous fibrin particles (Harrison, 1948 ; Muirhead and Montgomery, 1951 ; Bernard, 1953) and there seems to be no reason to suppose that they are other than thrombotic or embolic in origin. The widespread and random distribution of all the vascular lesions seems highly suggestive of thrombo-embolism and their close relationship to the connective tissue lesions suggests that they are the primary factor ; which, after all, is in accordance with the original views of Rose and Pillsbury (1939) Baehr, Klemperer, and Schifrin (1935) and Banks (1941).

The nature of the material deposited in the vessels is sometimes uncertain. Fibrin is most commonly involved but it is now recognized that other constituents of the blood may be deposited in the vessels as solid matter. Platelets are considered capable of forming intravascular occlusions in the " platelet thrombosis syndrome " (Fitzgerald, Auerbach and Frame, 1947 ; Gore, 1950 ; Biegelman, 1951) and it is significant that this syndrome has been accompanied in certain cases by tissue changes identical with those seen in systemic lupus erythematosus and dermatomyositis (Biegelman, 1951).

It has also been shown that abnormal globulins may be deposited as solid matter in the circulation (Muirhead, Montgomery and Gordon, 1952 ; Hansen and Farber, 1947). The identification of these by histological methods must depend on the elaboration of new histochemical or physical techniques.

Summary.

Three cases have been described which provide further evidence to reinforce the concept that systemic lupus erythematosus, scleroderma and dermatomyo-

sitis are separate clinical manifestations of one disease process. The vascular lesions are analysed and their relationship to the thrombosis hypothesis discussed.

I am indebted to Professor J. B. Duguid for his advice and encouragement and for his help in the preparation of the manuscript ; and to the clinicians in charge of the cases for allowing access to the case records.

References.

Baehr, G. and Pollack, A. D. (1947) *J. Amer. med. Ass.*, **134**, 1169.
——— Klemperer, P. and Schifrin, A. (1935) *Amer. J. Path.*, **11**, 881.
Banks, B. M. (1941) *New Engl. J. Med.*, **225**, 433.
Barnard, P. J. (1953) *J. Path. Bact.*, **65**, 129.
Biegelman, P. M. (1951) *Arch. Path.*, **51**, 213.
Crawford, T. and Levene, C. I. (1952) *J. Path. Bact.*, **64**, 523.
Duguid, J. B. (1946) *J. Path. Bact.*, **58**, 207.
——— (1948) *Ibid.*, **60**, 57.
——— (1949) *Lancet*, *ii*, 925.
——— (1952) *Ibid.*, *ii*, 207.
——— (1954) *Ibid.*, *i*, 891.
——— (1955) *Brit. med. Bull.*, **11**, 36.
——— and Robertson, W. B. (1955) *Lancet*, *i*, 525.
Fitzgerald, P. J., Auerbach, O. and Frame, E. (1947) *Blood*, **2**, 519.
Gore, I. (1950) *Amer. J. Path.*, **26**, 155.
Hansen, P. F. and Faber, M. (1947) *Acta med. scand.*, **129**, 81.
Harrison, C. V. (1948) *J. Path. Bact.*, **60**, 289.
Klemperer, P., Pollack, A. D. and Baehr, G. (1942) *J. Amer. med. Ass.*, **119**, 331.
Muirhead, E. E. and Montgomery, P. O'B. (1951) *Arch. Path.*, **52**, 505.
——— ——— and Gordon, C. E. (1952) *Arch. intern. Med.*, **89**, 41.
Pagel, W. and Treip, C. S. (1955) *J. clin. Path.*, **8**, 1.
Rannie, I. and Duguid, J. B. (1953) *J. Path. Bact.*, **66**, 395.
Rose, E. and Pillsbury, D. M. (1939) *Ann. intern. Med.*, **12**, 951.
Williams, G. (1955) *J. Path. Bact.*, **69**, 199.

OBSERVATIONS ON STEROID THERAPY IN PSORIASIS.

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Many workers, notably Grüneberg (1937) and Barber (1950), have suggested that there may be a relationship between psoriasis and adrenocortical hypofunction ; this has not been generally accepted, but it was inevitable that when steroids became available for treatment their effect in psoriasis would be investigated empirically. In this connection, although many reports have appeared, no great measure of agreement has yet been reached and indeed no long-term study has been published. Noguer Moré and Bassas Grau (1952) and Coste and his co-workers (1953) reported encouraging results in arthropathic psoriasis. In the series described in the first report of the Medical Research Council (1954) all except one of seven exfoliative cases improved, but a ready tendency to relapse was noted. On the other hand Hellier (1954) considered that the use of cortisone was not justified in psoriasis and Ingram (1954) found steroids of very limited value.

During the past three years we have assessed steroid therapy in fourteen cases of psoriasis which were selected because of the severity and extent of the condition. The findings are presented in Table I. All except Case 14 were treated with intramuscular injections of adrenocorticotropic hormone. Initial dosage varied from 100 mg. daily for $2\frac{1}{2}$ days to 150 mg. daily for 28 days and treatment was maintained with 20 mg. gel daily, except in Case 1 where 20 mg. gel every third day has been adequate. Case 14 received 60 mg. prednisolone daily for 12 days and this was reduced to a maintenance dose of 20 mg. daily. In three cases, treatment was discontinued because of complications : Agitated melancholia developed in Case 3, but a psychiatrist did not consider this to be due to therapy ; in Case 5, treatment was discontinued because of tiredness, weakness and cyanosis, with low serum potassium due to lack of co-operation in taking potassium orally, and the patient made a good recovery from coronary thrombosis ; in Case 8 vertebral collapse had no sequelae.

Table I.

Case No.	Age.	Type.	Duration of eruption (years).	Duration of treatment (days).	Result.
1	65	Arthropathic Exfoliative Bed-ridden	30	35	Skin well. Joint symptoms relieved. Moon face.
				260	Ambulant. Skin almost completely well. Joint symptoms relieved.
2	57	Plaque-like	1½	11	Skin well. Carbuncle developed. Psoriasis recurred 2 months later.
3	55	Plaque-like and exfoliative	30	10	Improved. Ankle oedema.
				40	Skin improved. Agitated melancholia.
				Off treat.	Developed generalized pustular phase.
				23	Marked improvement, then relapsed. Oedema still present.
				104	Deteriorated, gangrene of foot.
				Off treat.	Fall of serum proteins. (Total 3·5 g%).
				Off treat.	Died. P.M. Cerebro-vasc. degeneration, bronchopneumonia, exfoliative dermatitis.
4	37	Plaque-like	4⅓	52½	No benefit.
5	65	Widespread plaque-like	35	29	Skin well. Lumbosacral oedema. Moon face.
				70	Skin well. E.C.G.—flat T wave and ST depression lead II. Oedema still present.
				Off treat.	Coronary thrombosis. Exfoliative psoriasis.
6	47	Nummular and plaque-like	15	49	Much improved.
				130	Relapsed on reduction to 75 mg. daily.
7	40	Arthropathic plaque-like	11	52½	No benefit.
8	72	Arthropathic plaque-like	13	72½	Psoriasis cleared. Joint pains diminished.
				Off treat.	Relapsed 1 week later.
				93	Skin well. Slight ankle oedema.
				265	Developed severe low back pain. X-ray—collapse of D.X.
				Off treat.	Recurrence of psoriasis 1 week later.
9	23	Guttate and nummular	21	81	Cleared completely on 100 and 150 mg. dosage. Recurred completely on reduction of dose. Moon face, striae, hirsuties and acne vulgaris developed.
10	66	Flexural "seborrhoeic" pustular of hands and feet.	2½	73	Skin cleared completely. Then recurred on reduced dosage. Lumbar and ankle oedema.
				317	Much improved. Ankle oedema. E.C.G.—ST depression leads I and II.

TABLE I—*cont.*

Case No.	Age.	Type.	Duration of eruption (years).	Duration of treatment (days).	Result.
				396	Recurrence. Ankle oedema.
				458	Improved again on high dosage. Recurred at 50 mg. daily. Developed abscess at injection site. Ankle oedema.
11	16	Nummular and plaque-like	14	69	Regressed almost completely on top dosage and recurred on reduction of dose.
12	55	Generalized plaque-like	5	38	Cleared, then recurred.
				41	Improved somewhat.
13	60	Nummular and plaque-like	35	34	Cleared, then some recurrence on forearms, thighs and buttocks.
				219	Finally a few small areas of psoriasis on buttocks.
14	75	Widespread, exfoliative. Cardiac failure and oedema on admission	Life-long	73	Skin well, increasing oedema and cardiac failure.
				Off treat.	Slight relapse of psoriasis Gross oedema.
				28	A few lesions on limbs. No oedema.

COMMENT.

It is evident that steroid therapy is by no means a completely satisfactory form of treatment in psoriasis. There may, however, be an initial response in very chronic cases and in exfoliative states ; arthritic symptoms may be greatly benefited and severe relapses are uncommon. Prolonged local treatment with its attendant discomforts is obviated and a saving in clothing and bed-linen results. Conversely, the treatment is empirical and is apparently merely palliative in effect. Side-effects may be serious where prolonged use is necessary and too many contra-indications exist against the use of a merely palliative drug. The expense of treatment and also of the necessary investigative procedures is a serious drawback, but this may to some extent be set against economy in laundry and clothing.

It appears therefore, that although the present results are not entirely satisfactory, their importance lies in the demonstration that steroids exert a profound effect on inveterate cases of this disease. We believe that there is an indication for this form of treatment in such cases, especially when they are complicated by exfoliative changes and arthritis. It is probable that newer steroids will continue to be developed and already we have obtained encouraging results with the use of prednisolone. This is perhaps the dark age of steroids and the present blunderbuss of corticotropin or cortisone may finally be supplanted by a precision weapon that will direct itself to the parakeratotic or papillary target alone.

Summary.

The results of steroid therapy in fourteen severe cases of psoriasis are described and discussed.

Eight patients were maintained on treatment for periods varying from 73 days to 2 years $8\frac{1}{2}$ months and six received in-patient treatment for periods varying from 11 to 81 days.

References.

Barber, H. W. (1950) *Brit. med. J.*, *i*, 219.
Coste, F., Piguet, B. and Cayla, J. (1953) *Rev. Rhum.*, **20**, 208.
Grüneberg, T. (1937) *Arch. Derm. Syph., Wien*, **175**, 638.
Hellier, F. F. (1954) *Practitioner*, **172**, 503.
Ingram, J. T. (1954) *Brit. med. J.*, *ii*, 823.
Medical Research Council Report, Panel on Dermatological Applications of A.C.T.H. and Cortisone. (1954) *Brit. med. J.*, *ii*, 1307.
Noguer Moré, S. and Bassas Grau, E. (1952) *Act. dermo-sifilogr., Madr.*, **44**, 3.

LICHENOID DERMATITIS FOLLOWING GOLD THERAPY.

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Among the first observers of lichenoid lesions following gold therapy were Cardis and Conte (1936) who described a new clinical entity to which they applied the name "Chryscyanosis". They stated that it was characterized by a peculiarly persistent uniform pigmentation occurring on areas exposed to light. It usually began around the eyes and on the lids, later spreading to the forehead, but not involving the scalp. In a few cases the backs of the hands and forearms were affected Their series of cases (34) were undergoing treatment with gold preparations. Pigmentation usually occurred 2 or 3 years after cessation of treatment or when treatment was recommenced.

Sulzberger (1936) quoted a case described by Margarot *et al.* which presented features clinically resembling both psoriasis and lichen planus in a man who had received gold therapy three months previously. The eruption was papular with small white scales and the lesions were arranged in symmetrical rows radiating downwards and outwards from the spine. Although some of the lesions resembled lichen planus he concluded that this was a case of lichen hypertrophicus and consequently an "auride". Lichen planus-like lesions were also mentioned by Dowling (1945) either purely of a lichenoid character or associated with erythroderma. Occasionally the lichenoid lesions were seen only when the erythroderma was subsiding and they persisted for many months. Synder *et al.* (1939), in a review of 100 cases treated with gold salts observed one case that could be rightly grouped with those of Cardis and Conte.

In view of the extreme rarity of this dermatosis a more extensive review of the literature was carried out. In all, 1432 cases of rheumatoid arthritis treated with gold salts and reviewed by Smyth and Freyberg (1941), Hartfall *et al.* (1937), Fraser (1945), Dawson *et al.* (1941) and Cecil (1940) were studied, but no case of lichenoid dermatitis has been recorded by these authors in spite of a high percentage of skin reactions.

During the years 1946 to 1956, three cases of lichenoid dermatitis following gold therapy have been observed at the Western Infirmary, Glasgow, and cases are worthy of description in view of their rarity.

Case Reports.

Case 1.—A woman aged 32 was admitted to hospital on 2.vii.46.

During the 10 weeks before admission she had received in all 0·55 g. Myocrisin in five weekly doses of 0·05 g. and three weekly doses of 0·1 g. Within a few hours of

receiving the eighth injection she had become feverish and had several shivering attacks, and this had been followed by a widespread scarlatiniform eruption with intense itching. Three days later she had noted ulcers in her mouth and blisters on her abdomen.

When first seen on 2.vii.46 the patient had an extensive eczematous eruption involving the entire body, which in places, notably on the trunk, was becoming exfoliative. During the course of the next six weeks there was a steady improvement in her condition but the eczematous reaction persisted on the face and flexures, and the exfoliation on the trunk and limbs gave way to typical lichenoid lesions.

Face : The periorbital areas were mainly involved giving the impression from a distance of a bluish halo around the eyes. There were numerous bluish-grey oval lesions $\frac{1}{2}$ to $\frac{3}{4}$ inch by $\frac{1}{4}$ inch, with rather ill-defined borders and a tendency to coalesce. Grattage revealed fine silvery scaling, tending to form a collarette. There was a slight degree of infiltration and vitro-pressure showed no alteration in the general pigmentation.

Neck : Numerous bluish, oval and slightly infiltrated lesions were present, varying from $\frac{1}{2}$ to 1 inch in diameter ; fine silvery scaling was also present. The lesions had a necklace-like distribution, from the region of the seventh cervical vertebra spreading laterally downwards and forwards towards the sternal angle. No lesions were present between this line and the lower border of the mandible. Coalescence had occurred in places, notably on the lateral aspect of the neck.

Trunk : The pigmented lesions were widespread, tending to become confluent, especially marked in the mammary folds, suprapubic, inguinal and lumbo-sacral regions ; on the chest, abdomen and back they were discrete and well defined, slightly raised, circular or oval and varying in size from $\frac{1}{2}$ to $\frac{3}{4}$ inch in their long axis. On the anterior, posterior and lateral sides of the chest wall the lesions lay with their long axes parallel to the ribs as in pityriasis rosea.

Arms : The characteristic lesions were more numerous on the upper arms than on the forearms. They were discrete, oval, well defined, slightly infiltrated and scaly, but with no tendency to become confluent as elsewhere. No particular pattern or direction was taken up by the lesions. Similar pigmented lesions were present on the backs of both hands but not on the palms.

Legs : A few well defined pigmented lesions were scattered on the upper third of the inner aspects of the thighs but otherwise the legs were involved in a moist eczematous process.

Progress : The patient was discharged from hospital on 22.xii.46. A detailed examination was made four months later and it was found that the pigmented lesions on the limbs were gradually fading but those on the trunk were unchanged. Viewed against the light the lesions on the trunk appeared to be atrophic and slightly scaly ; when scales were removed an irregular silvery pattern was observed, slightly depressed and resembling lichen sclerosus.

When the patient was seen again in January 1948 it was noted that the limbs were clear but the lesions on the trunk were still well defined. They were no longer infiltrated and the pigmentation was breaking up in a retiform manner, the intervening areas being clinically atrophic.

Case 2.—A married woman aged 68, was admitted to hospital on 13.v.46 with an erythematous eruption following gold therapy for rheumatoid arthritis.

Myocrisin 0·5 g. had been given during January and February 1946 with no untoward effects and with considerable amelioration of her joint symptoms. In March 1946 she had complained of a red, itchy and scaly eruption of her face with swelling of the eyelids, and this was followed two days later by a similar eruption on her hands and feet.

On examination there was a widespread erythemato-squamous eruption which was almost confluent over both thighs, legs and arms, but less so on the hands

and feet. The lower abdomen and flexures were eczematized. Numerous pigmented lesions were scattered over the entire body surface.

On 2.vii.46 the erythema and scaling had subsided and a few discrete lichenoid lesions had now appeared on the arms, trunk, neck and abdomen. A marked increase of pigmentation had occurred in the periorbital areas and both eyelids were equally involved. The buccal mucosa was normal. The eruption resembled in many respects the tropical lichenoid dermatitis due to mepacrine.

On 30.viii.46 the following clinical picture was recorded :

Face : There was still marked periorbital pigmentation but no oedema. This discoloration appeared to be due to a coalescence of numerous bluish pigmented lesions which, on grattage, revealed fine silvery scales. Ill-defined pigmented lesions were present on the forehead, cheeks and upper lip tending to coalesce and form irregular pigmented patches with slight infiltration.

Neck : Numerous slightly raised pigmented lesions with slight infiltration were present, forming the characteristic necklace-like distribution which extended to the upper border of the sternum. On the sides of the neck several of the pigmented lesions had become confluent and formed an irregular well defined band.

Trunk : The skin appeared normal except for areas of pigmentation which were most marked on the flanks and abdomen and tended to coalesce forming regular, well defined patches in the mammary folds and inguinal region. On the front and back of the chest the lesions were fewer but well defined, measuring about $\frac{3}{4}$ to 1 inch by $\frac{1}{2}$ inch, with no infiltration but with fine silvery scaling. On the back of the chest the lesions lay with their long axes parallel to the ribs ; in the epigastric region they lay horizontally, and on the abdomen the long axes were directed downwards and inwards.

Legs : Pigmentation was most evident on the medial aspect of the upper third of the thighs and in these areas the lesions had coalesced to form well defined but irregular patterns varying in size from 3 to 5 inches in diameter on which scaling was most evident peripherally. The lower legs were eczematized in places, and only a few scattered pigmented macules could be seen.

Arms : The characteristic pigmentary changes were more numerous on the upper arms than on the forearms, oval or round, well defined and non-infiltrated. They were evenly distributed on all aspects of the upper arms with the exception of the medial and lateral aspects of the upper third where they coalesced to form pigmented areas which merged into those present in the axilae. Only a few irregularly distributed macules were present on the extensor aspects of the forearms and on the backs of the hands.

The patient was examined again on 6.i.47. The face was clear except for a bluish grey discoloration of the periorbital areas and of the upper and lower eyelids with slight fine silvery scaling. The necklace-like coalescence of the lesions was still pronounced. The abdomen, back, chest, legs and arms still showed the characteristic lesions but there was a tendency for them to be less well defined and paler on the forearms and backs of the hands. Viewed against the light most of the macules showed fine silvery stellate branching similar to lichen sclerosus.

Case 3.—A widow aged 69 was admitted to hospital on 14.ix.37.

While she was attending the Rheumatic Clinic a course of gold therapy had been started but only 0·33 g. of Myocrisin had been given when she developed an erythematous-squamous eruption involving her chest, abdomen, back and lower legs.

On admission to hospital she had a generalized erythemato-squamous eruption involving the flexor aspects of the forearms, axillae, mammary folds, abdomen, inguinal regions, medial aspect of the thighs, the sacral and popliteal regions.

Progress was uneventful and before she was discharged on 3.xi.37 it was observed that she showed a clinical picture similar to that described in Cases 1 and 2.

She died at the age of 74.

Discussion.

A consideration of these cases enable the recognition of a characteristic clinical syndrome the main features of which are :

(i) A history of gold therapy.
(ii) The appearance at an unpredictable date of a non-specific generalized erythematous, erythemato-papular or erythemato-squamous eruption with more or less eczematization of the axillae, inguinal, infra-mammary and retroauricular folds. This may resemble seborrhoeic dermatitis or a sensitization eruption and almost verge on exfoliative dermatitis.
(iii) Eczematous involvement of the scalp with diffuse thinning of the hair.
(iv) Periorbital oedema, either from the onset or as the eczematous process is subsiding.
(v) The appearance of characteristic lichenoid lesions following upon the gradual subsidence of the original eczematous process and gradually becoming evident through the predominating erythema.
(vi) The uniform bluish colour of the lesions, their uniformity in size and shape, and the silvery scaling on grattage.
(vii) The initial infiltration of the lesions which gradually becomes less evident until it is completely absent.
(viii) The unusual appearance of the pigmented lesions on the back of the the chest, and the tendency for the macules to lie with their long axes parallel to the ribs ; this feature is present, though not so striking, on the front of the chest.
(ix) The tendency for the areas that were originally eczematized, particularly the lower abdomen, sacral and inguinal regions, axillae, infra-mammary and retro-auricular folds to become more deeply pigmented, with coalescence of lesions.
(x) The characteristic *necklace-like* distribution of the lesions.
(xi) The bluish pigmentation of the periorbital areas and eyelids which, when viewed from a distance, appears to be almost confluent and very closely resembles a bruise.
(xii) The resistance to all forms of treatment and the eventual gradual fading of the pigmented macules on the limbs, starting on the backs of the hands.

There is a striking similarity between these features and those of lichenoid dermatitis following mepacrine (Nisbet, 1945; Peterkin and Hair, 1946; Bigham, 1946). Both syndromes show a non-specific eczematous process following the administration of the drug, and both proceed to the development of an unusual lichenoid stage with pigmented lesions of oval or circular contour, and atrophy. Other features common to both include :

(i) The necklace-like distribution.
(ii) The bluish colour of the lesions.
(iii) Residual areas of pigmentation where pigmentation had previously been most marked.
(iv) The presence of an almost uniform periorbital pigmentation.
(v) The shape and distribution of the lesions.
(vi) The atrophic stellate scarring of the lesions with fine silvery scaling.
(vii) The very marked coalescence of the lesions in the sacral region.

The striking clinical similarity is sufficient to point to a common aetiological factor, i.e. a drug, the ultimate effect of which is an eruption of the fixed type.

Summary.

Three cases of lichenoid dermatitis following gold therapy are described.
A characteristic clinical syndrome is recorded, and the striking similarity to tropical lichenoid dermatitis due to mepacrine is commented upon.

The material for this paper formed part of a Thesis for the degree of M.D. at the University of Glasgow.

References.

Bigham, A. (1946) *Brit. J. Derm. Syph.*, **58**, 271.
Cardis, F. and Conte, M. (1936) *Ann. Derm. Syph., Paris*, 7, sér. **7**, 229.
Cecil, R. L. (1940) *Proc. Mayo Clin.*, **15**, 556.
Dawson, M. H., Boots, R. H. and Tyson, T. L. (1941) *Trans. Ass. Amer. Phycns*, **56**, 330.
Dowling, G. B. (1945) *In Textbook of Medicine.* Edited by J. J. Conybeare. 7th ed. Edinburgh : E. & S. Livingstone Ltd., p. 1115.
Fraser, T.N. (1945) *Ann. rheum. Dis.*, **4**, 71.
Hartfall, S. J., Garland, H. G. and Goldie, W. (1937) *Lancet, ii*, 784.
Nisbet, T. W. (1945) *Arch. Derm. Syph., Chicago*, **52**, 221.
Peterkin, G. A. G. and Hair, H. C. (1946) *Brit. J. Derm. Syph.*, **58**, 263.
Smyth, C. J. and Freyberg, R. H. (1941) *Univ. Hosp. Bull. Mich.*, **7**, 45.
Synder, R. G., Traeger, C. and Kelly, L. (1939) *Ann. intern. Med.*, **12**, 1672.
Wise, F. and Sulzberger, M. B. (1936) *The* 1936 *Year Book of Dermatology and Syphilology.* Chicago : The Year Book Publishers Incorporated, p. 123.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. Louis Forman.

16 February 1956.

Alopecia Areata Treated with Hydrocortisone.—Dr. W. Frain-Bell for Dr. Oliver Scott.

Female, aged 11 years.

History.—Her first attack of alopecia areata developed at the age of 5 and lasted for $1\frac{1}{2}$ years. The second attack started 2 years ago, at first of limited extent, but becoming widespread during the summer of 1955. Active hair loss was still taking place in August 1955 when treatment with hydrocortisone was started. The process was confined to the scalp. No other member of the family had been similarly affected.

Treatment.—Hydrocortisone acetate in a dose of 10–15 mg. in 1 c.c. was injected into 6 separate areas of alopecia at monthly intervals. A 17-gauge needle was used and the solution introduced as far as possible into the upper dermis. On 2 occasions 1 mg. of hyaluronidase was added.

Results.—On each occasion regrowth of hair about 1–2 mm. in length was noted after 3–4 weeks at the site of injection. The hair was pigmented, not easily pulled out and the growth was progressive. Some spontaneous regrowth was first noted in the untreated areas in November 1955, i.e. 3 months after treatment was started.

Discussion.

The case was shown to demonstrate that local injection of hydrocortisone acetate could produce, in alopecia areata, progressive regrowth of pigmented hairs. Fifteen other cases have been similarly treated over a period, varying from 2 to 9 months, and in one instance only, a case of alopecia totalis, the ensuing regrowth was not maintained.

Postscript.

Since this patient was shown, we now have 50 others under observation, and the provisional impression gained is that in most of them growth of normally pigmented hair will occur at the site of injection, the growth being progressive but variable in degree, presumably depending on the severity of the active process. It does not occur after injection of hydraluronidase alone or of the fluid vehicle. Further prolonged observation will be necessary before any satisfactory conclusion can be drawn as the part that local injection of hydrocortisone might play in the treatment of alopecia areata, but it is likely that it will be a useful remedy for the most common type which Anderson (1950) found made up 70% of his cases, and that a reasonable cosmetic result can be achieved in anticipation of spontaneous regrowth.

The patient shown now has normal growth of scalp hair, except for 3 small bald patches. There has been no further active hair loss.

Reference.

Anderson, I. (1950) *Brit. med. J.*, ii, 1250.

Discussion.

Dr. N. A. Thorne : I consider that as well as injecting hydrocortisone one should inject a control lest the injection and not the hydrocortisone is stimulating hair growth.

I have injected a number of patients with hydrocortisone and although most have started to grow hair, as in this patient's case, the hair has not always continued to grow after injections have been stopped.

I feel it would be desirable to have a modified long-acting injection such as hydrocortisone with hyaluronidase so that repeated injections can be spaced over periods of 2 months.

Dr. Brian Russell : Hydrocortisone injections have undesirable side effects which should make us wary about this treatment. Sarcoid nodules can be flattened temporarily but ulceration may occur—a most unusual phenomenon in the natural course of the disease. Lichen planus hypertrophicus can be flattened and rendered non-pruritic, but atrophy remains and the skin becomes more vulnerable. In one patient the skin took on the yellow waxy appearance of necrobiosis. A biopsy confirmed the presence of necrosis, the biopsy wound broke down and healing was slow. To-day we see atrophy occurring in the skin of alopecia areata successfully treated with hydrocortisone injections. It is remarkable that this dermal atrophy is consistent with regrowth of the hair.

Dr. I. Martin-Scott : I have treated several such cases with injections of hydrocortisone. In each the result has been regrowth of hair about five deep around a small central depressed scar at the injection site. The new hair is pigmented from the start, but does not attain normal length, even after several months' observation.

Dr. J. Sommerville : When cortisone is given by the mouth, we have found within the 3 or 4 weeks mentioned, with a disease that has been resistant for years, there is remarkable strong, normal, pigmented hair growth. I have kept one patient on a maintenance dose, 20 mg. daily, and she has maintained her hair growth. I do not think it is increasing but it is remaining. It is extraordinary when on a permanently bald scalp, on which you think nothing will grow, a wonderful crop of pigmented hair grows after 3 or 4 weeks.

The President : It is very encouraging if the hair growth can be maintained with as little as 20 mg. of cortisone a day.

Dr. W. G. Tillman : I should like to ask Dr. Sommerville what dose he required for this case, because I have been singularly unsuccessful in growing hair in cases of alopecia when I have tried this treatment.

Dr. J. Sommerville : In one case it was 200 mg. and the other I pushed up to 400 mg. daily.

Dr. G. C. Wells : Injection of hydrocortisone crystals into the dermis may give rise to pseudo-atrophy with connective-tissue changes (Goldman, L., O'Hara, H. and Baskett, J. (1953) *J. invest. Derm.*, **20**, 271). It is therefore advisable not to inject large quantities (more than about 5 mg) into one site. May I ask Dr. Frain-Bell how large a zone of hair regrowth he would expect from a single injection of 10 or 20 mg. of hydrocortisone ?

Dr. Frain-Bell : A single injection of 10–15 mg. of hydrocortisone in 1 c.c. will produce an area of regrowth of hair at 3 to 4 weeks, of about 1½ cm. in diameter, but in some patients this area increases in size without further injection, with the passage of time. The amount of regrowth, however, varies from patient to patient.

Mercury Sensitivity Reaction in a Tattoo.—Dr. R. H. Meara.

T. L—, aged 21.

History.—In November 1954 he was tattooed on the right forearm. The subsequent inflammatory reaction subsided in the green and blue area but never cleared completely in the red ones. These have gradually become raised, scaly and irritable. He has had no other illnesses and there is no relevant family history.

On examination.—In a tattoo of the right forearm there are infiltrated erythematous areas showing some scaling. These skin changes are strictly confined to the red parts of the tattoo.

Biopsy of a red area.—There are many pigment granules scattered throughout the dermis. Most of the pigment appears to be within histiocytes some of which have formed foreign body giant cells. There are also dense collections of lymphocytes mainly around the small blood vessels. By transmitted light the granules appear brown.

Patch tests.

Patch tests were carried out as follows :—

Mercury perchloride, 1/10,000. Strongly positive at 48 hours.
Mercury biniodide, 1/10,000. Slightly positive at 48 hours.
Ung. Hydrarg. Ammon. B.P. Strongly positive at 48 hours.

Comment.

Beerman and Lane (1954) fully reviewed tattoo reactions. They collected 149 cases of which 102 were due to diseases transmitted during the procedure including 72 cases of primary syphilis and several cases of tuberculosis cutis and leprosy. They described 18 patients with mercury sensitivity reactions occurring only in the red areas and in which patch tests to mercury compounds, though not always to cinnabar, were positive.

Reference.

Beerman, H. and Lane, R. A. G. (1954) *Amer. Journ. Med. Sci.*, **227**, 444.

Discussion.

Dr. E. J. Moynahan : Has he any mercury filling in his teeth ?

Dr. Meara : He has one filling.

The President : Does a positive mercury patch test carried out at a distance lead to an eczematous response on the red area of the tattoo ?

Dr. Meara : That has been described but it is by no means always so. Of the 18 cases of mercury sensitivity collected by Beerman and Lane, only 2 or 3 showed this phenomenon.

The following cases have been published in *Proc. R. Soc. Med.*, **49**, 815.

Chronic Granuloma of the Gum with Swelling of the Lip in a Patient Handling Sodium Silicate Solution.—Dr. Louis Forman and Dr. C. W. Shuttleworth.

Chronic Granuloma of Mucous Membranes, and of the Lip and Chin ? Foreign Body Granuloma, ? Lupus Vulgaris.—Dr. Louis Forman and Mr. W. G. Cross.

Lichen Myxoedematosus.—Dr. Arthur Rook.

Granulomatous Cheilitis.—Dr. Arthur Rook and Dr. J. L. Moffatt.

Amyloidosis Cutis.—Dr. Arthur Rook and Dr. Danilo Stevanovic.

The following cases also were shown :

Psoriasis with Unilateral Facial Involvement. Milker's Nodes.—Dr. Mark Hewitt for Dr. Robert Warin.

Poikilodermia Atrophicans Vasculare.—Dr. C. H. Whittle and Dr. J. L. Moffatt.

Linear Lichen Planus.—Dr. R. H. Marten for Dr. Sydney Thomson.

Sarcoidosis with Dermatomyositis.—Dr. R. G. Howell and Dr. G. B. Mitchell-Heggs.

OXFORD DERMATOLOGICAL GROUP

6 October 1956.

Acrogeria. (Gottron Type).—Dr. H. T. Calvert.

A girl aged 6 years.

Family History.—Mother, father and brother aged 3—normal. No known skin disease of forebears. No consanguinity of parents.

Present History.—No illness during pregnancy of mother. A premature baby, birth weight 2 lb., she was kept in a maternity unit for three months and weighed 3 lb. when discharged. She said words at 9 months, walked alone without support at 10 months and was quite healthy as far as the parents could say, passing milestones normally. Her height was normal for her age and she did well at school. Appendicectomy was done in February 1956.

According to the mother, the wasted appearance of her hands and feet was noticed at birth. She is continually falling down, hurting herself and damaging the skin over her knees ; she bruises very easily. On one occasion she had to be admitted to hospital for laceration of her right knee. She is quick to get in a temper and throw herself about ; it is then that she so often injures herself.

On Examination.—Height 3 ft. 9 in. (114 cm.). Weight 2 st. 11 lb. (17·7 kg.).

Skin.—Although there is a general abnormality present the extremities show the greatest change. She has the emaciated fleshless hands and feet of an old woman with veins showing through the thin and wrinkled skin of the dorsa ; even the palms and soles show some loss of substance though they are much less affected. Her legs are like matchsticks below the knees, from loss of subcutaneous fat, and her wrists are likewise thin. Elsewhere the atrophy is less marked, but everywhere a lacework of blue veins shows through the skin. Her face partakes in the general wasting and her nose is thin and pinched. Her hands and feet are cold but there is no acrocyanosis. There are many scars over both kness and bruising is present on the thighs. There are no " tumours " on the knees.

Scalp hair, eyebrows and eyelashes are normal, and fine lanugo hairs present on limbs ; both big toe-nails are thickened. No abnormality of sweating.

General and ophthalmological examination.—Normal.

Investigations.—Skiagrams of epiphyses, wrist, elbow, knee and skull : Normal. Blood sugar (fasting) 55 mg. % ; (2 hours after glucose) 55. Twenty-four hour ketosteroids 0·8 mg./480 ml. urine. Biopsy not performed.

Comment.—First described by Gottron in 1940, only 4 cases have been reported. These concern 3 females and 1 male. The present case resembles very closely that described by Basex and Dupre (1955) who clearly differentiate acrogeria from other varieties of cutaneous atrophy, congenital or acquired.

References.

Gottron, H. (1940) *Arch. Derm. Syph.*, 181.
Gromzig, H. (1951) *Hautarzt*, **11**, 493.
Bazex, A. and Dupre, A. (1955) *Ann. Derm. Syph.*, **82**, 604.

Twenty-nine other cases also were shown by Dr. Calvert.

NOTICE.

THE BRITISH ASSOCIATION OF DERMATOLOGY

THIRTY-SEVENTH ANNUAL MEETING

At the thirty-seventh Annual Meeting of the Association to be held in London on Thursday 25, Friday 26, and Saturday 27 July 1957, the principle subjects for discussion will be "Sarcoidosis", "Disorders of Keratinization" and "Radioactive Isotopes in Dermatology".

BOOK REVIEWS.

Weberiana.*

This little book contains fifty-three pages in which Dr. Parkes Weber refers to, recounts, and discusses rare diseases and unusual patients in the way that is familiar to those who have studied his previous books. This is followed by a very erudite 13-page essay on Paracelsus.

Finally comes a most interesting letter which he wrote in 1953 to the President of the Royal Numismatic Society. In the course of the letter one gathers that his interest in the rare and unusual was not confined to the study of medicine. He began to collect coins in 1880, and mention is made of a communication to the *Numismatic Chronicle* in 1892.

Fortunately for all of us, he did not give up medicine when he gave up collecting coins in 1906.

F. R. B.

Treatment.*

In this booklet are published nine contributions on therapy of skin disease delivered to a meeting of the South-West German Dermatologists in October 1955. One describes the treatment of psoriasis with folic acid and another that of lichen planus with vitamin D_3. Here we shall wait for confirmation. Otherwise the views generally conform to our own. The authors set out to be more critical than has been customary in the German literature but it is admitted that one of the causes of a more critical attitude lies in the sheer multitude of preparations now being offered for therapy.

M. F.

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* *Interesting Cases and Pathological Considerations.* By F. Parkes Weber (1956). London: H. K. Lewis & Co. Ltd. Pp. 77. Illus. 5. Price 18*s*. 6*d*.

* *Heutiger Stand der Therapie der Hautkrankheiten.* Edited by Dr. E. Landes (1956). Berlin-Göttingen-Heidelberg. Springer Verlag. Pp. 95. Illus. 24. Price Rm. 12.60.

An Introduction To Dermatology.*

Let it be said at once that this book has many excellent features, particularly in the general discussions on treatment and diagnosis. " The history of a case of skin-disease as obtained from the patient is of little importance except when it is confined to simple facts " and " the absence of itching is of more importance than its presence " are but two examples of many statements of facts which only too rarely receive recognition. Unfortunately many of the criticisms made in this journal about the earlier edition still remain valid. Of course, dermatologists differ in their interpretations and this is more likely to occur where different schools with their different traditions are concerned. Nevertheless it is felt that some changes would be for the better and the following remarks are intended to be constructive ; merely indicating some of the points, they do not constitute a detailed criticism.

Lichen planus papules are described as " diamond-shaped " and it is true that they are always polygonal. But they rarely assume the simple outline of a diamond ; the excellent illustration on page 165 demonstrates this point. Perhaps this is a variant of the Curse of Scotland. There is no reference to deltacortisone in the treatment of this disease.

Although cats and mice are mentioned in the section on favus, only " animals " receive some recognition in the section on tinea capitis. In the treatment of fungous infections the use of 3% salicylic acid and 5% benzoic acid receives frequent mention but nothing is said of the equally important penetrating base used in the real Whitfield's ointment. Most dermatologists would not use thallium acetate as a treatment for scalp ringworm.

Intertrigo is apparently included under " Infective Eczema ", the name itself receiving no recognition despite the fact that eczematous changes are by no means always present, e.g. under the breasts.

Bismuth is omitted from the treatment of lupus erythematosus : " X-ray and Radium Dermatitis " is dismissed somewhat casually : Basin's disease is boldly classed with the sarcoids. Although it is now recognized that molluscum sebaceum is by no means rare the condition is not included, whereas such real rarities as blastomycosis and sporotrichosis have their paragraphs and their illustrations. No attention is drawn to the great differences between the juvenile and adult forms of urticaria pigmentosa.

There is a 3-page chapter on Tropical Diseases, covering eight conditions but yet failing to mention prickly heat.

It is of course always most difficult to decide what shall or shall not be included in an " Introduction " but surely there is no point in dragging in glomus tumour, only for it to be dismissed in two or three lines ; or the poikilodermas, to receive a similar fate.

There are terms which the reviewer frankly dislikes, e.g. vitropression and unguem. Some arrangements, too, are difficult to understand. Thus " Keratodermia climactericum " is dealt with in the chapter on dystrophies. Reference is there made to page 135 : this seems to be a misprint for page 138 where there is an illustration of " Keratosis climacterica ", this occurring in the chapter on eczema and dermatitis.

Although the volume is generously illustrated some of the coloured plates could be improved ; but appreciation of colour is a personal possession which varies from one individual to another both in its detection and in its analysis. The publishers deserve the greatest praise for their part of the production. We have however learned to expect this very high standard from Messrs. Livingstone. S. T.

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* *An Introduction to Dermatology.* By G. H. Percival (1956). Edinburgh : E. & S. Livingston Ltd. 12th edition. Pp. 374. Illus. 256, 188 in colour. Price 45*s.* net.

CURRENT LITERATURE

THE CLINICAL SIGNIFICANCE OF CERTAIN DISTURBANCES IN SWEATING. M. B. Sulzberger. (1956) *Dermatologica*, **112**, 161.

The author deals with two aspects of the secretion and delivery of sweat and the disturbances of these functions. In his first section he discusses the sweat-retention syndrome which arises from the impairment of the delivery of sweat. In his second section he goes more fully into the mutual relationship between the sweat and the sebum and fatty substances on the skin. He explains the influence of sweating on the delivery and spreading of the lipoid substances on the skin surface, and the part played by the sweat as emulsifier for the fatty substances. On the basis of experimental studies made in the author's institution by Franz Herrmann and co-workers, he supports the concept that the total lipoids of the skin surface are composed of two parts: one, a smaller part, which forms a thin surface film over the horny layer: and the second and larger part which is found in the cracks and clefts of the deeper stratum corneum and in the follicle openings as a receptacle: and from this receptacle flows on to the surface according to demand. Finally, the significance of these processes in the protective functions of the skin against infection is emphasized, as well as their roles in relation to climate, to too fatty and too dry skin, senile skin, chapping, etc. (Author's summary.) J. F. S.

KERATOSIS FOLLICULARIS SERPIGINOSA (LUTZ). J. Marshall and H. I. Lurie. (1956) *Dermatologica*, **113**, 13.

(1) The literature on keratosis follicularis serpiginosa (elastoma intrapapillare penetrans verruciforme) is reviewed.

(2) An additional case has been described in detail.

(3) Histological studies show that the primary lesion is the rupture of hair follicles (due perhaps to ingrowing lanugo hairs) and possibly sweat ducts.

(4) The presence of an "elastoma" as postulated by Miescher is disputed.

(5) It is shown that the condition bears no histological resemblance to Kyrle's disease. (Authors' summary.) J. F. S.

SCABIES NORVEGICA AND LYMPHATIC LEUKAEMIA, WITH REPORT OF A HOSPITAL EPIDEMIC OF ATYPICAL SCABIES. A. Dostrovsky, F. Raubitschek and F. Sagher. (1956) *Dermatologica*, **113**, 26.

A patient with lymphatic leukaemia suffered simultaneously from scabies norvegica. The clinical picture of the skin was one of erythrodermia, which can be due to both diseases. Skin sections showed infiltrations of lymphatic leukaemia and revealed the presence of sarcoptes scabiei. Following treatment for scabies, the erythroderma improved, and it is therefore assumed that scabies norvegica was its main cause. A hospital epidemic occurred among 25 contacts but no mites could be detected in them either by direct search or in serial sections of two biopsy specimens. (Authors' summary.) J. F. S.

THE SIGNIFICANCE OF IRON IN THE SKIN FOR THE DIAGNOSIS OF HAEMOCHROMATOSIS. W. Soltermann. (1956) *Dermatologica*, **112**, 335.

Haemosiderin can be found in normal skin. but owing to autolysis it disappears rapidly on cooling, so that biopsy specimens should be fixed while still at body temperature, and necropsy specimens are liable to show none. The considerable variations both in health and in haemochromatosis impose caution in interpreting results. J. F. S.

"KISSING-BUG" BITE. T. L. Shields and E. N. Walsh. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **74**, 14.

In America the "Kissing bug" is not only a phenomenon of psychogenic origin but may be a genuine arthropod, one of several species of Triatoma, about 1 cm. long and thus easily visible to the naked eye. The actual bite is usually not perceived (hence the name), but the reaction may be severe and include systemic manifestations. The "Kissing-bug" may be a vector of one form of trypanosomiasis. J. K.

PORPHYRINS, PORPHYRINURIA AND PORPHYRIA. Israel Zeligman. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **74**, 33.

PHOTOSENSITIVITY IN VARIOUS DERMATOSES. Beatrice Maher Keston. (1956) *A.M.A. Arch. Derm. Syph. Chicago.*, **74**, 40.

THE KOEBNER PHENOMENON IN ITS RELATIONSHIP TO PHOTOSENSITIVITY. Paul Gross. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **74**, 43.

PROTECTION OF THE SKIN AGAINST THE HARMFUL EFFECTS OF SUNLIGHT. Norman B. Kanof. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **74**, 46.

These four papers were contributed to a symposium on photosensitivity in dermatology. The first is useful for its graphic formulae of the porphyrins. The second deals with lupus erythematosus, urticaria due to light and polymorphic light eruptions in a very brief and orthodox manner. In the third article Koebner's phenomenon is considered to be a reaction to various stimuli where there is a disturbance of cellular metabolism in the skin. Actinic rays take their place as suitable stimuli along with mechanical and chemical irritation. The last article divides local protectors against the sun into sun " shades " which mechanically prevent the rays reaching the skin and sun " screens " which absorb the rays and dissipate their energy in a harmless manner. The value of systemic measures against the harmful effects of sunlight is still unsettled.

J. K.

PEMPHIGUS VULGARIS : A CORRELATION OF CLINICAL AND MICROSCOPIC OBSERVATIONS. Isadore Fisher. (1956) *A.M.A. Arch. Derm. Syph., Chicago.*, **74**, 50.

The author concludes that there is no correlation between clinical and histological diagnosis. There is no clear cut difference in the course or prognosis of cases showing intraepidermal (acantholytic) and subepidermal (non-acantholytic or tension) bullae. Both types of bullae may be found at different times in the same patient. All should be labelled " pemphigus "; there is no call for a sub-class of " senile dermatitis herpetiformis " or " pemphigoid ".

(It is a pity that this article should have been so carelessly compiled. Paragraphs are repeated with only slight verbal change and two of the Tables are identical except that the words " consecutive " and " serial " are exchanged in the titles. Statements made do not appear consistent from one part of the article to another and the inferences do not appear always to be soundly drawn. This makes one less willing to accept the author's conclusions.) J. K.

ALLERGIC HYPERSENSITIVITY TO AN ANTISEPTIC SOAP. I. H. Blank. (1956) *J. Amer. med. Ass.*, **160**, 1225.

A new antiseptic soap contains tetramethylthiuram disulphide, which is also used in the rubber industry as an accelerator. Patch-testing 5 patients known to be allergically sensitive to thiuram sulphide compounds with the soap itself and in 8% solution provoked a vesicular reaction. Although the possibility of users of the soap developing an allergic sensitivity must be remembered, it appears to be a very rare occurrence in practice. A. J. R.

AGRANULOCYTOSIS AND SCARLATINIFORM ERUPTION DUE TO PHENINDIONE. B. H. Pastor and A. F. Tetreault. (1956) *J. Amer. med. Ass.*, **161**, 873.

Agranulocytosis, a rare complication of anticoagulant therapy with phenindione, was accompanied by a generalized scarlatiniform eruption. A. J. R.

CHRONIC POSTHERPETIC NEURALGIA. L. S. Van Blaricom and G. Horrax. (1956). *J. Amer. med. Ass.*, **161**, 511.

Postherpetic neuralgia affects men and women equally and is very uncommon before the age of 40. Thirty-five patients with neuralgia of more than 3 years' duration were studied and the response to many types of treatment was assessed. The precise mode of production of the pain is unknown ; the authors suggest that the virus causes extensive and persistent inflammatory changes which are the original source of the pain ; when the central nervous system is bombarded by pain inpulses for too long a period a central pain mechanism is established, with self-perpetuating circuits. Adequate analgesics to relieve pain during the initial attack are therefore important. The chronic neuralgia is seldom helped by medicines and seldom improves spontaneously. Many minor and major surgical techniques are described and evaluated. A. J. R.

ALOPECIA AREATA DUE TO SYPHILIS. H. T. Behrman and S. T. Wild. (1956) *J. Amer. med. Ass.*, **161**, 726.

Syphilitic alopecia may take the form of alopecia areata ; such an occurrence is reported in a man aged 28. The great ease with which the hair can be removed from almost any part of the scalp should raise the suspicion of syphilis. A. J. R.

LONG-TERM MANAGEMENT OF PEMPHIGUS VULGARIS WITH CORTICOTROPIN (ACTH). R. B. Stoughton. (1956). *J. Amer. med. Ass.*, **160**, 1011.

Pemphigus vulgaris in 9 patients has been successfully controlled with ACTH. All patients are well and are leading active lives except one who died of coronary thrombosis and one who is incapacitated by disseminated sclerosis. The control of pemphigus for an indefinite period seems practicable, as 5 of the patients have now received ACTH for $1\frac{1}{2}$ to $4\frac{1}{2}$ years, with only occasional periods in hospital, and there has been no evidence of any failure of suprarenal response. In the last 3 years a purified corticotropin-gel has been given daily or on alternate days or 3 times weekly. The daily maintenance dose has varied from 15 to 80 units. A. J. R.

DIFFUSE HAIR LOSS ASSOCIATED WITH SELENIUM (SELSUN) SULFIDE SHAMPOO. R. W. Grover. (1956) *J. Amer. med. Ass.*, **160**, 1397.

Brief histories are given of six patients who developed diffuse hair loss after regular use of Selsun shampoo for periods ranging from 5 weeks to about 3 years. The hair regrew when the shampoo was stopped. The author suggests that the hair loss may be a toxic effect of the absorption of the selenium ion. A. J. R.

THE TREPONEMA PALLIDUM IMMOBILIZATION TEST, A DIAGNOSTIC AID TO THE CLINICIAN. R. K. Ledbetter, Jr. (1956) *J. Amer. med. Ass.*, **160**, 1392.

The T.P.I. test is most useful as a verification test, particularly in the diagnosis of latent syphilis, as it eliminates both false-positive and false-negative serological reactions. It has little value as a test of cure. A. J. R.

SIGNIFICANCE OF THE TREPONEMA PALLIDUM IMMOBILIZATION TEST ON SPINAL FLUID. J. L. Miller, M. H. Slatkin and J. H. Hill. (1956) *J. Amer. med. Ass.*, **160**, 1394.

Levels of treponemal immobilizing antibodies are usually lower in the cerebrospinal fluid than in the blood. Positive T.P.I. tests are diagnostic of neurosyphilis but negative tests may not exclude the diagnosis. A. J. R.

SENSITIZATION TO FACIAL TISSUES WITH UREA-FORMALDEHYDE RESIN (WET-STRENGTH). S. M. Peck and L. L. Palitz. (1956) *J. Amer. med. Ass.*, **160**, 1226.

The soft paper tissues used by women to remove cosmetics are sometimes impregnated with urea-formaldehyde resins to give them greater strength when wet. These resins are potential sensitizers. A. J. R.

NEUROLOGICAL AND PSYCHIATRIC SIGNS ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS. R. C. Clark and A. A. Bailey. (1956) *J. Amer. med. Ass.*, **160**, 455.

Of 100 patients with systemic lupus erythematosus 24 showed neurological abnormalities and 17 psychic disturbances. These changes were usually not attributable to steroid therapy, uraemia or hypertension and were presumably produced by involvement of the blood vessels supplying brain or spinal cord. Transient involvement of any part of the nervous system may appear during the course of systemic lupus erythematosus. A. J. R.

PREDNISONE AND PREDNISOLONE IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS. E. L. Dubois. (1956) *J. Amer. med. Ass.*, **161**, 427.

For the dermatologist who has to treat only a small number of cases of systemic lupus erythematosus each year this is a particularly helpful article. Thirty-seven patients were treated with prednisone or prednisolone. Both preparations were approximately five times as effective, dose for dose, as cortisone. The median daily maintenance dose was 2 mg. Patients receiving over 10 mg. daily should be on an ulcer regimen to avoid the 22% incidence of peptic ulcer. Patients receiving over 50 mg. daily require a low sodium diet as prednisone is as liable to cause sodium retention as cortisone, although it develops more slowly. On very high doses the most serious risk is the

production of diabetes. The therapeutic efficacy of these drugs in lupus erythematosus is equivalent to that of cortisone. A. J. R.

SOME ASPECTS OF OCCUPATIONAL DERMATOSES. J. V. Klauder. (1956) *J. Amer. med. Ass.*, **160**, 442.

This long and thoughtful article should be read by all who are interested in occupational skin disease. Primary irritants (27·7%) trauma and accidental injury and their sequelae (22·1%) sensitizers (15·2%) and wet work (15·0%) were the most frequent causes established in 2,407 cases. Problems of diagnosis are discussed, including difficulties in the interpretation of patch-tests. The so-called non-specific polyvalent sensitization, which has been invoked to explain the chronicity of certain cases, is merely a fashionable modern term for the old " status eczematosus " and is really no more precise or explicit. Except through cross-sensitization to chemically related substances, it is not established that a specific cutaneous sensitivity predisposes to the development of further sensitization. Prognosis, and the many factors influencing it, are fully considered. A. J. R.

INTERSTITIAL PNEUMONITIS IN DERMATOMYOSITIS. E. S. Mills and W. H. Mathews. (1956) *J. Amer. med. Ass.*, **160**, 1467.

In a fatal case of dermatomyositis in a woman aged 52 pulmonary symptoms ushered in the disease and predominated throughout its course. At post-mortem examination interstitial pneumonitis with fibrosis was present. The diagnosis of dermatomyositis appears to be unquestionable. A. J. R.

NOBECUTAN IN DERMATOLOGY. E. Keinig and G. Weber. (1956) *Derm. Wschr.*, **133**, 393.

There are many references to nobecutan as a dressing in surgery, but its use in dermatology has been neglected up to now. This substance is investigated from various points of view. It is tolerated well by both normal and diseased skin; therapeutic agents remain in contact with the skin for up to 10 days after fixation by nobecutan; perspiration is possible through the nobecutan film; treatment of dermatoses with tar and cignolin fixed with nobecutan is satisfactory; and the substance affords protection from irritants in industrial dermatitis. W. G. T.

ENDOGENOUS ECZEMA AND NEPHROTIC SYNDROME. G. W. Korting. (1956) *Derm. Wschr.*, **133**, 406.

Report of a case of asthma-eczema associated with nephrosis. There was a family history of eczema and kidney disease. Despite the absence of reference to the association of these two conditions the author considers that there is an aetiological connexion. The association is well known in the paediatric literature. W. G. T.

A COMBINED THERAPY IN ERYTHRODERMIA DESQUAMATIVA (LEINER). G. Bugyi. (1956) *Derm. Wschr.*, **133**, 417.

Since the introduction of a combined therapy with steroids, choline chloride and vitamin B complex in addition to the previous local therapy with borax-glycerine, the mortality from this condition has significantly decreased. W. G. T.

PELLAGRA IN INH-THERAPY. W. Gockell. (1956) *Derm. Wschr.*, **133**, 448.

First symptoms of pellagra occurred after 3·7 gm. of INH given for lupus vulgaris of the palate. Owing to failure to recognize the early manifestations further INH up to 6·1 gm. was given and after prolonged exposure to sunlight the full picture developed which was then recognized and treated with nicotinic acid amide, folic acid and pantothenic acid. Complete recovery occurred after 14 days. When further INH therapy was required by the patient injections of nicotinic acid amide and a diet rich in vitamin B prevented a recurrence of pellagra. W. G. T.

CURE OF TWO CASES OF NECROSIS PROGRESSIVA SUBCUTANEA NEONATORUM. G. Bugyi. (1956) *Derm. Wschr.*, **133**, 497.

This condition first described by Feer is characterized by progressive subcutaneous connective tissue necrosis in the newborn or during the first weeks of life. It is usually seen in premature infants and is probably due to trophic disturbances. The author was able to save two infants

in both of whom the sacral region was affected by transfusions and antibiotics as well as careful feeding and nursing care. W. G. T.

HISTOCHEMICAL INVESTIGATION FOR ZINC IN PSORIATIC SKIN. O. Braun-Falco and B. Rathjens. (1956) *Derm. Wschr.*, **134**, 837.

Zinc is probably important for enzyme action and protein synthesis. In animal experiments lack of zinc can produce loss of pigment, disturbances of hair growth and in the rats a squamous dermatosis with acanthosis and parakeratosis. A lack of zinc capable of reacting with the reagent used was also found in 11 of 14 cases of psoriatic skin examined. Of other dermatoses examined only lichenification showed diminution. The similarity between the manifestation in rats and human psoriasis is of interest, though psoriasis is not claimed to be due to general lack of zinc but rather to a localized disturbance in zinc metabolism resulting perhaps in an insufficient utilization of zinc by the cells of the epidermis. W. G. T.

THE ERNST FUCHS SYNDROME. R. Frühwald. (1956) *Derm. Wschr.*, **136**, 841.

Under this title the author describes a case of ulceration of the cornea, hypopyon and iritis later developing erosions of the nose and ears and ulcers and nodules on buttocks and thighs as well as vesicles on the fingers. The patient died of lymphatic leukaemia. The association of this syndrome, which is of the type described by Behcet, with other diseases is well known.
W. G. T.

LIGHT URTICARIA IN PORPHYRINURIA. R. Schmitz and W. Wagner. (1956) *Derm. Wschr.*, **134**, 765.

Porphyrinuria was suspected in a case of light urticaria on account of the presence of other symptoms such as severe constipation, migraine and minor epileptic manifestations. It was stressed that only the fourth examination of the urine revealed porphyrins. It is not claimed that urticaria of the light sensitivity type is another porphyrin disease but porphyrins present in urticarial patients may precipitate an attack. W. G. T.

THE ROLE OF LARGACTIL IN THE TREATMENT OF SOME DERMATOSES. St. Racz and Z. Gallai. (1956) *Derm. Wschr.*, **134**, 770.

Largactil was found ineffective in psoriasis, it was most useful in suppressing the itching of eczematous conditions though the clinical appearance of the condition was not materially affected. The drug failed to suppress vesicles produced artificially with monoiodoacetic acid.
W. G. T.

PATHOLOGICAL X-RAY FINDINGS IN TIBIA AND FIBULA IN VARICOSE ULCERS. E. Hobl. (1956) *Derm. Wschr.*, **134**, 746.

Fifty-eight of 100 cases of varicose ulceration without any arterial changes showed x-ray abnormalities. Sometimes these were not very striking. They consisted in osteoplastic changes of the periosteum either underlying the ulcer or at some distance from it. A control series of 50 cases of the same age group showed no changes except occasionally in those over 70.
W. G. T.

BESNIER'S PRURIGO. Oscar Gans. (1956) *Actas dermo-sif, Madrid*, **47**. 543.

Gans reviews the various opinions expressed on the cause of this disorder, one that is apparently increasing in Europe and North America. Most of the patients are leptosomic in type, i.e. ectomorphs. In affected flexures the capillaries are generally contracted, there is a lower uptake of oxygen by the epidermal cells which contain less calcium and magnesium than normal . There is also no doubt about a connection between Besnier's prurigo and the nervous system, particularly the vegetative one ; though whether the initial reaction is that of the skin on the nervous system or vice versa is uncertain. Gans thinks that there is probably a familial and constitutional inferiority which affects the vital capacity of the skin and lessens its resistance to harmful stimuli.

General treatment is directed to the patient as a whole and to the nervous system in particular. Largactil and Atosil seem to be useful. ACTH and cortisone are used either to deal with a very grave stage or when the patient shows some tendency to spontaneous improvement. Unfortunately cortisone lowers the calcium balance which should be compensated. Tar is the best local medicament, and can advantageously be combined with 1/8–1/4% hydrocortisone. G. W. B.